JAMA Neurology | Original Investigation | GLOBAL BURDEN OF DISEASE

Global, Regional, and National Burden of Nontraumatic Subarachnoid Hemorrhage
The Global Burden of Disease Study 2021

GBD 2021 Global Subarachnoid Hemorrhage Risk Factors Collaborators

IMPORTANCE Nontraumatic subarachnoid hemorrhage (SAH) represents the third most common stroke type with unique etiologies, risk factors, diagnostics, and treatments. Nevertheless, epidemiological studies often cluster SAH with other stroke types leaving its distinct burden estimates obscure.

OBJECTIVE To estimate the worldwide burden of SAH.

DESIGN, SETTING, AND PARTICIPANTS Based on the repeated cross-sectional Global Burden of Disease (GBD) 2021 study, the global burden of SAH in 1990 to 2021 was estimated. Moreover, the SAH burden was compared with other diseases, and its associations with 14 individual risk factors were investigated with available data in the GBD 2021 study. The GBD study included the burden estimates of nontraumatic SAH among all ages in 204 countries and territories between 1990 and 2021.

EXPOSURES SAH and 14 modifiable risk factors.

MAIN OUTCOMES AND MEASURES Absolute numbers and age-standardized rates with 95% uncertainty intervals (UIs) of SAH incidence, prevalence, mortality, and disability-adjusted life-years (DALYs) as well as risk factor–specific population attributable fractions (PAFs).

RESULTS In 2021, the global age-standardized SAH incidence was 8.3 (95% UI, 7.3-9.5), prevalence was 92.2 (95% UI, 84.1-100.6), mortality was 4.2 (95% UI, 3.7-4.8), and DALY rate was 125.2 (95% UI, 110.5-142.6) per 100 000 people. The highest burden estimates were found in Latin America, the Caribbean, Oceania, and high-income Asia Pacific. Although the absolute number of SAH cases increased, especially in regions with a low sociodemographic index, all age-standardized burden rates decreased between 1990 and 2021: the incidence by 28.8% (95% UI, 25.7%-31.6%), prevalence by 16.1% (95% UI, 14.8%-17.7%), mortality by 56.1% (95% UI, 40.7%-64.3%), and DALY rate by 54.6% (95% UI, 42.8%-61.9%). Of 300 diseases, SAH ranked as the 36th most common cause of death and 59th most common cause of DALY in the world. Of all worldwide SAH-related DALYs, 71.6% (95% UI, 63.8%-78.6%) were associated with the 14 modeled risk factors of which high systolic blood pressure (population attributable fraction [PAF] = 51.6%; 95% UI, 38.0%-62.6%) and smoking (PAF = 14.4%; 95% UI, 12.4%-16.5%) had the highest attribution.

CONCLUSIONS AND RELEVANCE Although the global age-standardized burden rates of SAH more than halved over the last 3 decades, SAH remained one of the most common cardiovascular and neurological causes of death and disabilities in the world, with increasing absolute case numbers. These findings suggest evidence for the potential health benefits of proactive public health planning and resource allocation toward the prevention of SAH.

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Supplemental content

Group Information: GBD 2021 Global Subarachnoid Hemorrhage Risk Factors Collaborators appear at the end of the article.

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Nontraumatic subarachnoid hemorrhage (SAH) represents the third most common stroke type after ischemic stroke and intracerebral hemorrhage, accounting for 5% to 10% of all strokes.[1,2] Of all nontraumatic SAHs, approximately 85% are caused by the rupture of an intracranial aneurysm, which distinguishes its etiology, risk factors, symptoms, diagnostics, treatments, and outcomes from other types of stroke.[3] Even though comprehensive SAH-specific burden and risk factor estimates would be crucial for its accurate evidence-based health care planning and resource allocation, SAH is still frequently clustered with other stroke types leaving its unique epidemiology and prevention strategies obscure.

Consistent with various population-based studies worldwide,[4-6] a recent Global Burden of Diseases (GBD) 2021 stroke study reported that the age-standardized burden rates of SAH and other stroke types decreased globally with a substantial geographical variation.[2] However, because the study focused mainly on stroke in general,[2] many SAH-specific findings such as its rankings against the burden estimates of other critical health outcomes were not reported. Therefore, we decided to use the GBD 2021 dataset and focus solely on the global, regional, and national burden of SAH and its risk factors over the last 3 decades. Primarily, we hypothesized that even though the age-standardized burden rates of SAH are decreasing, they still consist of a substantial proportion of the burden related to cardiovascular, neurological, and noncommunicable diseases. This article was produced as part of the GBD Collaborator Network, and in accordance with the GBD protocol.[7]

Key Points

Question What is the global burden of nontraumatic subarachnoid hemorrhage (SAH)?

Findings Results of this cross-sectional study, based on the Global Burden of Disease 2021 study, reveal that in 2021, there were 700 000 new SAH cases, almost 8 million patients with prevalent SAH, 350 000 SAH deaths, and over 10 million SAH-related disability-adjusted life-years globally. Despite decreasing age-standardized burden rates, SAH remained one of the most common cardiovascular and neurological causes of death and disability in the world.

Meaning Given the high proportional burden of SAH, study results suggest evidence for the potential health benefits of proactive public health planning and resource allocation for SAH prevention.

Methods

Overview

Details of the GBD methodology are presented elsewhere.[8,9] In brief, GBD studies have been conducted since 1990 to provide annual standardized burden estimates of critical health outcomes and their attribution to behavioral, environmental, and metabolic risks worldwide. By aiming to use all available evidence via its repeated cross-sectional study design, the GBD studies use censuses, household surveys, vital registrations, administrative data collections, disease registers, verbal autopsy tools, air pollution monitors, satellite imaging, and scientific literature as its primary data sources. Based on the actual data points and relevant predictive covariates, the final and missing data are further estimated using various statistical models for fatal and nonfatal burden estimates (eAppendix, eMethods, and eTable 1 in Supplement 1). Because the data sources and assessments of the whole time series are reevaluated and updated in pursuance of every annual release, the latest GBD results supersede the preceding estimates. In the most recent data release, the GBD 2021 study used over 607 billion data points to illustrate the annual burden of 371 diseases and injuries as well as 88 risk factors from 204 countries and territories between 1990 and 2021. The exact data sources are publicly available through the website of the Institute for Health Metrics and Evaluation.[10] Because GBD studies rely on the analysis of aggregated secondary data without the direct involvement of human subjects, individual studies based on the publicly available database do not require separate approvals from institutional review boards or informed consent from individuals whose health conditions are studied. The reporting of this manuscript followed the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) recommendations.[11]

SAH Definition and Data Sources

In line with the definition of the World Health Organization, the GBD 2021 study defines SAH as a nontraumatic stroke type caused by bleeding into the subarachnoid space of the brain. This definition includes first-ever SAHs with aneurysmal and nonaneurysmal origins but excludes recurrent SAHs and secondary SAHs caused by intracranial traumas. Correspondingly, the study uses primarily code 430 from the *International Classification of Diseases, Ninth Revision* (*ICD-9*) and code I60 from the *Tenth Revision* (*ICD-10*) to identify relevant data sources and outcomes. According to the 4-level categorization of the GBD studies, SAH belongs to the most specific level 4 category being also part of the categories of noncommunicable diseases (level 1), cardiovascular diseases (level 2), and strokes (level 3). Overall, the GBD 2021 study comprises 2563 data sources for fatal SAHs, 311 data sources for nonfatal SAHs, and 36 data sources for SAH risk factors from 132 different countries/regions between 1963 and 2022 (eAppendix, eMethods, and eFigures 1-4 in Supplement 1).

Risk Factor Estimation

Similar to causes, the GBD classifies risk factors into 4 different levels from the broadest level 1 to the most detailed level 4. For SAH, the GBD 2021 study has available data for all 3 risk clusters of level 1 and 14 individual risk factors from levels 2 to 4 (eAppendix, eMethods, and eTable 2 in Supplement 1). To evaluate the association of 3 risk clusters and 14 available risk factors with SAH-specific burden, the GBD 2021 study uses a comparative assessment framework to calculate population attributable fractions (PAFs) defined as a theoretical proportion of burden that could be prevented by changing the expo-

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sure of the risk to the theoretical minimum risk exposure level in the population (eAppendix and eMethods in Supplement 1).[12]

Statistical Analysis

Based on the available data input sources and assumptions of geospatial relationships between relevant covariates such as smoking prevalence, systolic blood pressure, and lag distributed income per capita, the GBD uses primarily 2 statistical modeling tools, namely, cause of death ensemble modeling (fatal estimates) and disease-model bayesian meta-regression 2.1 (nonfatal estimates), to produce annual burden estimates of SAH across different population groups and geographical locations between 1990 and 2021 (Appendix, eMethods, and eTable 1 in Supplement 1).[8,9] Consistent with previous GBD stroke reports,[2,13,14] we used the absolute numbers and age-standardized (adjusted to the age structure of the GBD standard population) rates per 100 000 people of 4 outcomes to illustrate the burden of SAH as follows: (1) incidence, (2) prevalence, (3) deaths, and (4) DALYs (eAppendix, eMethods, and eTable 3 in Supplement 1). According to the cause-specific number of deaths and DALYs, we also compared the absolute burden of SAH within 3 stroke types, 11 neurological disorders including strokes, 18 cardiovascular diseases, 192 noncommunicable diseases, and 300 individual diseases/injuries on the same hierarchy level with associated deaths or DALYs (eAppendix, eMethods, and eTable 3 in Supplement 1). To present the attributions of risk factors to SAH-related DALY estimates, we presented the age-standardized PAFs in percentages and DALY rates per 100 000 people attributed to each included risk factor or cluster. Besides average global estimates in 2021, we presented all burden estimates with 95% uncertainty intervals (UIs) and stratified by sex, 4 age groups, 5 Sociodemographic Index (SDI) levels, 7 GBD super regions, 21 GBD regions, and 204 individual countries and territories (eAppendix, eMethods, and eTable 3 in Supplement 1). Lastly, we evaluated the temporal trends by comparing the burden and risk factor estimates between 1990 and 2021. All analyses of the current study are based on the publicly available GBD results[15] and visualization tools.[16] Data were analyzed from 1990 to 2021.

Results

Global Burden of SAH in 2021

Based on the overall global estimates, we observed 0.7 (95% UI, 0.6-0.8) million new SAH cases, 7.9 (95% UI, 7.2-8.6) million patients with prevalent SAH, 0.4 (95% UI, 0.3-0.4) million SAH deaths, and 10.6 (95% UI, 9.4-12.1) million SAH-related DALYs in 2021 (**Table 1**). These resulted in the age-standardized SAH incidence of 8.3 (95% UI, 7.3-9.5), prevalence of 92.2 (95% UI, 84.1-100.6), mortality of 4.2 (95% UI, 3.7-4.8), and DALY rate of 125.2 (95% UI, 110.5-142.6) per 100 000 people. Although the prevalence of SAH was higher in female individuals than in male individuals, the point estimates of other age-standardized burden figures were higher in male patients (Table 1). The rates of all burden estimates of both sexes increased along with increasing age (Table 1 and eFigure 5 in Supplement 1).

Regional and National Burden of SAH in 2021

All age-standardized burden estimates of SAH varied substantially between 204 countries and territories worldwide (**Figure 1** and eTables 4-11 in Supplement 1). By SDI level, we found the highest age-standardized prevalence as well as the lowest mortality and DALY rates of SAH in high-SDI regions (eTable 5 in Supplement 1). On the other hand, the highest age-standardized incidence, mortality, and DALY rates occurred in low-middle- and middle-SDI regions (eTable 5 in Supplement 1). According to the 7 GBD super regions, we found the lowest age-standardized mortality and DALY rates in North Africa and the Middle East, Sub-Saharan Africa, and high-income super regions, whereas the lowest incidence rates were observed in North Africa, the Middle East, and Sub-Saharan Africa. Latin America and the Caribbean had, in turn, the highest age-standardized rates of all 4 burden estimates (eTable 5 in Supplement 1). These geographical differences also varied slightly between male and female individuals (eTables 6 and 7 in Supplement 1) as well as between different age groups (eTables 8-11 in Supplement 1). In high-SDI regions, we observed that female individuals had higher incidence, prevalence, mortality, and DALY rates compared with males, but these differences were not observed in other SDI regions.

Temporal Changes in SAH Burden

Between 1990 and 2021, the absolute number of annual new SAH incidents increased from 0.5 to 0.7 million (37.1%; 95% UI 32.2%-42.4%) and prevalent cases from 4.9 to 7.9 million (60.2%; 95% UI, 56.9%-63.4%). Moreover, the absolute number of global deaths and DALYs due to SAH had an increasing trend since 2005 (**Figure 2**A). However, according to the age-standardized rates per 100 000 people, all burden estimates of SAH decreased worldwide between 1990 and 2021, with incidence from 11.7 to 8.3 (28.8%; 95% UI, 25.7%-31.6%), prevalence from 109.9 to 92.2 (16.1%; 95% UI, 14.8%-17.7%), mortality from 9.5 to 4.2 (56.1%; 95% UI, 40.7%-64.3%), and DALY rate from 275.9 to 125.2 (54.6%; 95% UI, 42.8%-61.9%) (Figure 2B and eTable 12 in Supplement 1). Although the absolute number of new SAH incidents and prevalence increased among all SDI levels, the increases were more evident in low- and low-middle-SDI regions where the absolute number of deaths and DALYs also increased over the whole study period (eFigure 10 and eTables 13 and 14 in Supplement 1). Moreover, we found decreasing age-standardized burden estimates in all SDI categories, but the decreases were the most evident in middle- and high-middle-SDI regions (eFigure 10 and eTables 15 and 16 in Supplement 1).

SAH Burden Compared With Other Causes

Of 300 level 4 diseases/injuries modeled by the GBD 2021 study, SAH ranked as the 36th most common cause of death (0.5%; 95% UI, 0.5%-0.6% of all deaths) and 59th most common cause of DALY (0.4%; 95% UI, 0.3%-0.4% of all DALYs) in the world (**Figure 3**). The corresponding rankings were 23rd and 39th among 192 noncommunicable diseases, 6th and 6th among 18 cardiovascular diseases, and 5th and 6th among 11 neurological disorders including strokes (eTable 17 in Supplement 1). We observed the highest rankings and proportional burdens of SAH

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Table 1. Global Number and Age-Standardized Rates With 95% Uncertainty Intervals (UIs) of Subarachnoid Hemorrhage Incidence, Prevalence, Mortality, and Disability-Adjusted Life-Years (DALYs) in 2021[a]

Group	Incidence	Prevalence	Mortality	DALY
Overall				
Absolute No. in millions (95% UI)	0.70 (0.61-0.80)	7.85 (7.16-8.58)	0.35 (0.31-0.40)	10.64 (9.40-12.12)
Age-standardized rate per 100 000 people (95% UI)	8.33 (7.34-9.48)	92.17 (84.08-100.60)	4.18 (3.66-4.76)	125.20 (110.54-142.61)
Female				
Absolute No. in millions (95% UI)	0.36 (0.32-0.41)	4.31 (3.95-4.69)	0.18 (0.16-0.21)	5.16 (4.62-5.89)
Age-standardized rate per 100 000 people (95% UI)	8.17 (7.21-9.35)	97.88 (89.66-106.58)	3.91 (3.41-4.55)	116.35 (104.22-133.10)
Male				
Absolute No. in millions (95% UI)	0.34 (0.30-0.39)	3.54 (3.22-3.89)	0.17 (0.14-0.22)	5.48 (4.50-6.90)
Age-standardized rate per 100 000 people (95% UI)	8.51 (7.48-9.65)	85.52 (77.67-93.74)	4.48 (3.64-5.56)	134.07 (109.87-167.87)
Children (0-14 y)				
Absolute No. in millions (95% UI)	0.034 (0.023-0.046)	0.21 (0.17-0.25)	0.0033 (0.0026-0.0041)	0.31 (0.25-0.37)
Rate per 100 000 people (95% UI)	1.67 (1.16-2.29)	10.27 (8.49-12.50)	0.16 (0.13-0.20)	15.29 (12.34-18.51)
Young adults (15-49 y)				
Absolute No. in millions (95% UI)	0.24 (0.19-0.30)	2.71 (2.43-3.04)	0.055 (0.047-0.067)	3.19 (2.74-3.82)
Rate per 100 000 people (95% UI)	6.13 (4.83-7.50)	68.63 (61.46-76.87)	1.39 (1.19-1.69)	80.75 (69.42-96.78)
Old adults (50-74 y)				
Absolute No. in millions (95% UI)	0.29 (0.24-0.37)	3.97 (3.55-4.42)	0.17 (0.15-0.20)	5.49 (4.85-6.26)
Rate per 100 000 people (95% UI)	17.90 (14.67-22.24)	241.76 (216.37-268.90)	10.57 (9.25-12.15)	334.32 (295.19-381.09)
Very old adults (≥75 y)				
Absolute No. in millions (95% UI)	0.13 (0.10-0.16)	0.97 (0.83-1.11)	0.12 (0.10-0.14)	1.66 (1.43-1.86)
Rate per 100 000 people (95% UI)	44.35 (35.94-54.15)	334.57 (286.56-386.05)	41.93 (35.80-47.51)	573.62 (494.79-643.62)

[a] The results are presented overall and separately for female and male individuals and 4 age groups.

in many middle-SDI regions such as Latin America and East Asia but also in the high-income Asian Pacific. The lowest rankings and proportional burdens occurred in low-SDI regions, especially in Sub-Saharan Africa (eTables 18 in Supplement 1).

Risk Factors Attributed to SAH Burden

Of all worldwide SAH-related DALYs in 2021, 71.6% (95% UI, 63.8%-78.6%) attributed to the 14 modeled risk factors by the GBD study (**Table 2**). By the 3 level 1 risk clusters, metabolic risks accounted for the most risk-attributed DALYs of SAH, followed by the environmental/occupational risks and behavioral risks (Table 2 and eFigure 6 in Supplement 1). The top 3 individual risk factors were high SBP (PAF = 51.6%; 95% UI, 38.0%-62.6%), smoking (PAF = 14.4%; 95% UI, 12.4%-16.5%), and ambient particulate matter pollution (PAF = 14.2%; 95% UI, 9.8%-18.0%). The rankings varied slightly between male and female individuals (eFigure 7 in Supplement 1). By SDI levels, the attribution of all risk factors combined to SAH-related DALYs was highest in the low-SDI level (PAF = 77.3%; 95% UI, 70.2%-82.7%) and the lowest in the high-SDI level (PAF = 64.3%; 95% UI, 52.3%-74.0%). This was mainly attributed to the increased proportion of environmental/occupational risks and especially the increase in the association of household air pollution, which was attributed to 35.8% (95% UI, 28.5%-42.9%) of the SAH-related DALYs in the low-SDI level and less than 0.1% (95% UI, 0-0.3%) of the SAH-related DALYs in the high-SDI level (eFigures 6-8 in Supplement 1). Between 1990 and 2021, the age-standardized DALY rate of SAH that attributed to all risk factors combined decreased by 56.6% (95% UI, 44.7%-63.7%), and this decrease was more evident in environmental/occupational and behavioral risks than in metabolic risks (Table 2).

Discussion

According to the GBD 2021 study estimates, in 2021, there were 700 000 new SAH cases, almost 8 million patients with prevalent SAH, 350 000 SAH deaths, and over 10 million SAH-related DALYs globally. This ranked SAH as the 36th most common cause of death and 59th most common cause of death and disability in the world among 300 critical health outcomes. Although the global age-standardized mortality and DALY rates of SAH more than halved during the last 3 decades, the absolute number of patients with prevalent SAH increased by over 60% during the same period. This increase reached 105% in low-SDI levels where the absolute number of SAH-related deaths and disabilities also increased by more than 50%. Al-

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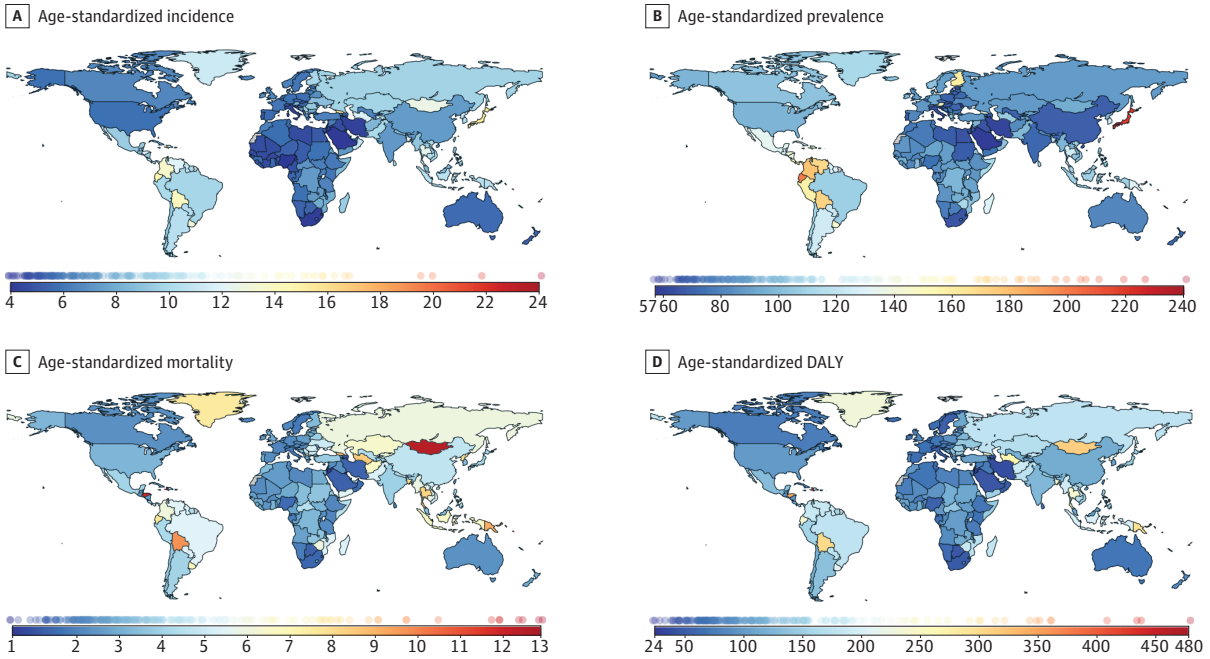
Figure 1. Worldwide Burden of Subarachnoid Hemorrhage in 2021



Age-standardized incidence (A), prevalence (B), mortality (C), and disability-adjusted life-years (DALYs) (D) rates of subarachnoid hemorrhage per 100 000 people in 204 countries and territories in 2021. The circles above the scales represent the estimates from individual countries. Figure created with The Institute for Health Metrics and Evaluation, Global Burden of Diseases Study 2021.[16]

though these increases may be partially explained by improved diagnostic and documentation of SAH cases, some of these increases can be attributed to increased aging and population growth offering opportunities to reduce globally increasing SAH-related health consequences through improved prevention strategies. Without such urgent, international, and interdisciplinary actions, we can expect the absolute burden of SAH to continue to increase, particularly in low-SDI regions.

Observations about decreasing incidence and mortality rates of SAH are consistent with previous systematic reviews and pooled analyses of individual population-based cohort studies around the world.[4-6] Such favorable trends have mainly been related to the decreasing prevalence of smoking,[5,17] improved management of hypertension,[5] improved management of SAH (eg, shortened treatment delays, increasing access to neurointensive care units, and evolvements of endovascular aneurysm treatments),[18] as well as improvements in the pre-SAH interventions of persons with unruptured intracranial aneurysms (UIAs).[5,19] Notably, most of these findings originate from high-SDI regions, whereas low- and middle-SDI areas continue to face significant challenges in accessing and delivering quality health care services for patients with SAH. For example, approximately 90% of the countries in GBD regions such as Sub-Saharan Africa, East Asia, and Oceania have been reported to lack urgent access to advanced microneurosurgery.[20] In comparison with population-adjusted figures, previous literature on trends of absolute SAH cases, deaths, and disabilities is limited yet such estimates act as a cornerstone of worldwide public health planning and resource allocation. According to a recent policy view by the World Stroke Organization,[21] the absolute burden of SAH was predicted to increase by over 40% by 2050, which was more than the corresponding estimates of other stroke types. However, although the policy view[21] introduced extensive pragmatic solutions to reduce the global burden of stroke overall by improving its surveillance, prevention, acute care, and rehabilitation, the recommendations did not consider any SAH-specific characteristics. For instance, lower median age, female predisposition, distinct etiologies, high sudden-death rates, and unique neurosurgical treatment modalities of SAH as well as prevention possibilities of persons with UIAs were not assessed. Similarly, other key prevention guidelines on stroke, cardiovascular diseases, and neurological disorders have clustered all stroke types disregarding the distinct features of SAH,[22-25] whereas the SAH-specific guidelines have focused on in-hospital diagnostics and management rather than prevention strategies of SAH.[3,26,27] Given the distinct characteristics of SAH, its substantial proportion of global health burden, and large attribution to modifiable risk factors, guidelines on SAH-specific primary, secondary, and tertiary prevention that also consider the patients and high-risk individuals outside of the neurosurgical tertiary care are warranted in the future.

Besides surpassing the burden of most cardiovascular diseases (eg, atrial fibrillation/flutter, aortic aneurysms, heart valve diseases, peripheral arterial diseases, endocarditis, and myocarditis) and neurological disorders (eg, Parkinson disease, ten-

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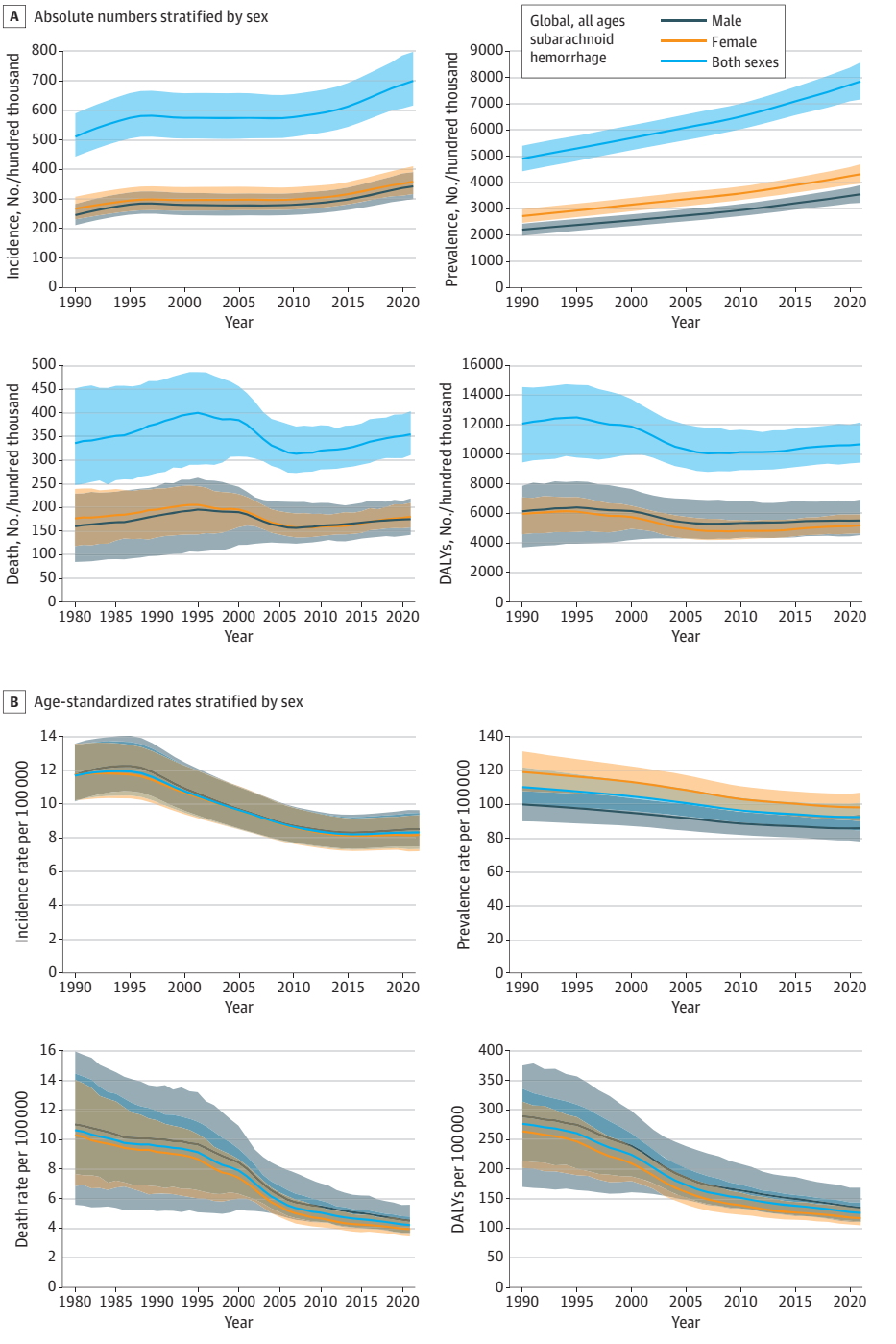
Figure 2. Changes in the Incidence, Prevalence, Deaths, and Disability-Adjusted Life-Years (DALYs) of Subarachnoid Hemorrhage in the World Between 1990 (Deaths Since 1980) and 2021



Results are presented as absolute number (A) and age-standardized rates (B) per 100 000 people as well as stratified by sex. Solid lines represent the changes in point estimates, and shaded areas represent 95% uncertainty intervals. Figures created with The Institute for Health Metrics and Evaluation, Global Burden of Diseases Study 2021.[15]

sion-type headache, motor neuron diseases, and multiple sclerosis), the global number of SAH deaths and disabilities also exceeded various other life-threatening infections (eg, encephalitis, hepatitis, and deaths due to meningitis), cancers (eg, brain, prostate and cervical cancers, leukemias and lymphomas), and injuries (eg, physical violence by firearms and sharp objects, sexual violence and nature disasters). Given that most of these causes in GBD studies are combinations of various 3-character *ICD* health conditions, our findings suggest that SAH is not only a common but also one of the most common cardiovascular and neurological causes of death and disabilities. Similarly high proportional burdens have also been reported in previous studies,[28,29] which is understandable given the relatively low median age of SAH combined with high sudden-death, short-term case-fatality, and morbidity rates. For example, according to a previous nationwide study from

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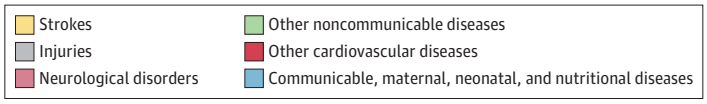
Figure 3. The Most Common Causes of Death and Disability-Adjusted Life-Years (DALYs) in the World in 2021



Cause of death	Ranking	% of All deaths (95% UIs)
Ischemic heart disease	1	13.25 (12.27-13.87)
COVID-19	2	11.63 (10.79-12.48)
Chronic obstructive pulmonary disease	3	5.48 (4.96-5.92)
Ischemic stroke	4	5.29 (4.78-5.64)
Intracerebral hemorrhage	5	4.87 (4.49-5.19)
Other COVID-19 pandemic-related outcomes	6	3.96 (3.10-5.23)
Lower respiratory infections	7	3.22 (2.94-3.44)
Tracheal, bronchus, and lung cancer	8	2.97 (2.71-3.20)
Alzheimer disease and other dementias	9	2.88 (0.75-7.39)
Type 2 diabetes	10	2.37 (2.21-2.48)
Hypertensive heart disease	11	1.96 (1.66-2.15)
Diarrheal diseases	12	1.72 (1.19-2.37)
Drug-susceptible tuberculosis	13	1.54 (1.35-1.76)
Colon and rectum cancer	14	1.54 (1.42-1.63)
Stomach cancer	15	1.41 (1.22-1.57)
Falls	16	1.18 (1.00-1.28)
Malaria	17	1.10 (0.40-2.28)
Neonatal preterm birth	18	1.09 (0.93-1.27)
Self-harm by other specified means	19	1.02 (0.94-1.08)
Breast cancer	20	0.99 (0.92-1.05)
Neonatal encephalopathy due to birth asphyxia and trauma	21	0.89 (0.76-1.04)
Esophageal cancer	22	0.79 (0.71-0.88)
HIV/AIDS resulting in other diseases	23	0.76 (0.67-0.87)
Pancreatic cancer	24	0.75 (0.68-0.79)
Chronic kidney disease due to type 2 diabetes	25	0.70 (0.60-0.83)
Chronic kidney disease due to hypertension	26	0.67 (0.56-0.77)
Pedestrian road injuries	27	0.65 (0.58-0.70)
Motor vehicle road injuries	28	0.64 (0.60-0.69)
Asthma	29	0.64 (0.53-0.82)
Prostate cancer	30	0.64 (0.56-0.69)
Chronic hepatitis B including cirrhosis	31	0.64 (0.55-0.73)
Parkinson disease	32	0.57 (0.52-0.61)
Rheumatic heart disease	33	0.55 (0.48-0.65)
Chronic hepatitis C including cirrhosis	34	0.54 (0.47-0.63)
Cirrhosis due to alcohol	35	0.52 (0.44-0.61)
Subarachnoid hemorrhage	36	0.52 (0.45-0.59)
Atrial fibrillation and flutter	37	0.50 (0.43-0.54)
Chronic kidney disease due to other and unspecified causes	38	0.45 (0.38-0.52)
Other cardiomyopathy	39	0.45 (0.41-0.49)
Urinary tract infections and interstitial nephritis	40	0.44 (0.40-0.48)
Cervical cancer	41	0.44 (0.41-0.47)
Drowning	42	0.40 (0.38-0.43)
Other non-Hodgkin lymphoma	43	0.38 (0.35-0.41)
Brain and central nervous system cancer	44	0.38 (0.33-0.43)
Congenital heart anomalies	45	0.37 (0.31-0.45)
Motorcyclist road injuries	46	0.35 (0.31-0.38)
Neonatal sepsis and other neonatal infections	47	0.34 (0.29-0.39)
Paralytic ileus and intestinal obstruction	48	0.34 (0.30-0.38)
Peptic ulcer disease	49	0.34 (0.29-0.40)
Other malignant neoplasms	50	0.33 (0.30-0.35)
Bladder cancer	51	0.33 (0.30-0.36)
Other neonatal disorders	52	0.33 (0.23-0.39)
Other cardiovascular and circulatory diseases	53	0.33 (0.30-0.36)
Meningitis	54	0.32 (0.26-0.39)
Lip and oral cavity cancer	55	0.31 (0.28-0.32)
Chronic kidney disease due to glomerulonephritis	56	0.29 (0.24-0.33)
Protein-energy malnutrition	57	0.28 (0.25-0.31)
Interstitial lung disease and pulmonary sarcoidosis	58	0.28 (0.24-0.31)
Ovarian cancer	59	0.27 (0.25-0.29)
HIV/AIDS - drug-susceptible tuberculosis	60	0.27 (0.21-0.33)
Liver cancer due to hepatitis B	61	0.27 (0.22-0.32)
Endocrine, metabolic, blood, and immune disorders	62	0.26 (0.23-0.28)
Cirrhosis due to other causes	63	0.26 (0.20-0.31)
Gallbladder and biliary tract cancer	64	0.25 (0.21-0.29)
Physical violence by firearm	65	0.25 (0.24-0.27)
Kidney cancer	66	0.24 (0.22-0.25)
Alcohol use disorders	67	0.23 (0.19-0.25)
Aortic aneurysm	68	0.23 (0.20-0.25)
Liver cancer due to hepatitis C	69	0.22 (0.18-0.25)
Physical violence by other means	70	0.21 (0.20-0.22)
Nonrheumatic calcific aortic valve disease	71	0.21 (0.18-0.23)
Idiopathic epilepsy	72	0.21 (0.17-0.22)
Gallbladder and biliary diseases	73	0.19 (0.17-0.23)
Acute myeloid leukemia	74	0.19 (0.17-0.22)
Pancreatitis	75	0.18 (0.16-0.21)

Cause of DALY	Ranking	% of All DALYs (95% UIs)
COVID-19	1	7.37 (6.54-8.25)
Ischemic heart disease	2	6.55 (5.90-7.17)
Lower respiratory infections	3	2.87 (2.48-3.24)
Neonatal preterm birth	4	2.79 (2.44-3.13)
Chronic obstructive pulmonary disease	5	2.77 (2.47-3.03)
Intracerebral hemorrhage	6	2.76 (2.46-3.04)
Other COVID-19 pandemic-related outcomes	7	2.69 (2.06-3.61)
Type 2 diabetes	8	2.61 (2.34-2.92)
Ischemic stroke	9	2.44 (2.19-2.68)
Low back pain	10	2.42 (1.86-3.06)
Diarrheal diseases	11	2.05 (1.65-2.50)
Neonatal encephalopathy due to birth asphyxia and trauma	12	2.03 (1.73-2.33)
Malaria	13	1.91 (0.78-3.71)
Tracheal, bronchus, and lung cancer	14	1.62 (1.41-1.82)
Major depressive disorder	15	1.59 (1.14-2.12)
Other musculoskeletal disorders	16	1.56 (1.17-2.05)
Age-related and other hearing loss	17	1.53 (1.14-2.00)
Falls	18	1.52 (1.33-1.71)
Migraine	19	1.49 (0.23-3.15)
Drug-susceptible tuberculosis	20	1.48 (1.30-1.67)
Anxiety disorders	21	1.47 (1.06-1.91)
Alzheimer's disease and other dementias	22	1.26 (0.62-2.64)
Dietary iron deficiency	23	1.12 (0.81-1.50)
Self-harm by other specified means	24	1.08 (0.97-1.18)
HIV/AIDS resulting in other diseases	25	1.02 (0.90-1.17)
Hypertensive heart disease	26	0.88 (0.74-0.99)
Motor vehicle road injuries	27	0.86 (0.80-0.93)
Colon and rectum cancer	28	0.85 (0.76-0.93)
Neonatal sepsis and other neonatal infections	29	0.81 (0.70-0.94)
Stomach cancer	30	0.79 (0.68-0.92)
Congenital heart anomalies	31	0.77 (0.64-0.93)
Asthma	32	0.74 (0.63-0.90)
Pedestrian road injuries	33	0.74 (0.66-0.82)
Breast cancer	34	0.72 (0.65-0.78)
Neck pain	35	0.71 (0.50-0.94)
Other neonatal disorders	36	0.70 (0.51-0.85)
Alcohol use disorders	37	0.59 (0.49-0.70)
Other gynecological diseases	38	0.55 (0.39-0.72)
Drowning	39	0.55 (0.49-0.61)
Schizophrenia	40	0.51 (0.38-0.65)
Meningitis	41	0.50 (0.39-0.65)
Motorcyclist road injuries	42	0.49 (0.43-0.53)
Chronic hepatitis B including cirrhosis	43	0.48 (0.40-0.56)
Idiopathic epilepsy	44	0.48 (0.38-0.59)
Rheumatic heart disease	45	0.47 (0.41-0.54)
Esophageal cancer	46	0.45 (0.39-0.52)
Endocrine, metabolic, blood, and immune disorders	47	0.45 (0.36-0.57)
Osteoarthritis knee	48	0.41 (0.21-0.80)
Chronic hepatitis C including cirrhosis	49	0.41 (0.34-0.49)
Protein-energy malnutrition	50	0.41 (0.35-0.47)
Near vision loss	51	0.40 (0.18-0.76)
Autism spectrum disorders	52	0.40 (0.28-0.56)
Chronic kidney disease due to other and unspecified causes	53	0.40 (0.36-0.43)
Pancreatic cancer	54	0.39 (0.35-0.44)
Chronic kidney disease due to type 2 diabetes	55	0.39 (0.33-0.45)
Opioid use disorders	56	0.39 (0.32-0.45)
Cirrhosis due to alcohol	57	0.39 (0.32-0.46)
Chronic kidney disease due to hypertension	58	0.38 (0.32-0.44)
Subarachnoid hemorrhage	59	0.37 (0.32-0.43)
Other congenital birth defects	60	0.37 (0.30-0.49)
Dysthymia	61	0.36 (0.24-0.49)
Physical violence by firearm	62	0.35 (0.32-0.38)
Other cardiovascular and circulatory diseases	63	0.35 (0.31-0.40)
HIV/AIDS - Drug-susceptible tuberculosis	64	0.34 (0.27-0.42)
Cervical cancer	65	0.34 (0.31-0.39)
Physical violence by other means	66	0.33 (0.31-0.36)
Edentulism	67	0.33 (0.23-0.43)
Other exposure to mechanical forces	68	0.32 (0.26-0.38)
Other mental disorders	69	0.31 (0.21-0.44)
Brain and central nervous system cancer	70	0.31 (0.27-0.36)
Other unintentional injuries	71	0.30 (0.23-0.36)
Conflict and terrorism	72	0.30 (0.25-0.38)
Other cardiomyopathy	73	0.30 (0.26-0.33)
Fire, heat, and hot substances	74	0.29 (0.24-0.34)
Atrial fibrillation and flutter	75	0.29 (0.25-0.34)

Rankings of the 75 most common causes of death and DALYs in the world in 2021 presented as percentages with 95% uncertainty intervals.

Finland,[28] aneurysmal SAH represented the 18th most common cause of death in middle-aged people (40-64 years old). By similar age stratification in the GBD 2021 study, consistent findings occurred not only in Finland but also in other Nordic and Western European countries with universal health care, and registration structures emphasizing the substantial role of SAH among the most common causes of premature mortality in working-age individuals (eFigure 9 in Supplement 1).

In line with various population-based cohort studies reporting not only associative[30-33] but also causal relationships,[34-37] high SBP and smoking were the 2 leading risk factors with the largest attribution to the burden of SAH. Because our findings suggest that eliminating these 2 risk factors would more than halve the burden of SAH, their prioritization is justified when placing prevention strategies for SAH. For example, advertisement bans, age restrictions, increased

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Table 2. Age-Standardized Proportions, Absolute Numbers, and Age-Standardized Rates of Subarachnoid Hemorrhage (SAH)–Related Disability-Adjusted Life-Years (DALYs) Attributed to Risk Factors in 2021 and Their Changes Between 1990-2021

Risk factors	Age-standardized proportion of SAH-related DALYs attributed to risk factors		Absolute number of SAH-related DALYs attributed to risk factors		Age-standardized SAH-related DALY rate per 100 000 people attributed to risk factors	
	In 2021, PAF (95% UI)	Change between 1990 and 2021, % (95% UI)	In 2021, No. in millions (95% UI)	Change between 1990 and 2021, % (95% UI)	In 2021, rate per 100 000 (95% UI)	Change between 1990 and 2021, % (95% UI)
All risk factors	71.54 (63.17 to 76.16)	−4.31 (−9.28 to −0.69)	7.72 (6.52 to 9.11)	−10.97 (−25.53 to 12.05)	89.60 (75.68 to 105.80)	−56.59 (−63.73 to −44.65)
Behavioral risks	28.69 (19.40 to 38.78)	−21.44 (−32.59 to −12.40)	3.11 (2.08 to 4.32)	−28.15 (−43.50 to −5.46)	35.96 (23.98 to 49.92)	−64.42 (−71.68 to −52.92)
Diet high in red meat	−7.03 (−29.02 to 9.97)	11.16 (−7.28 to 65.75)	−0.75 (−3.10 to 1.06)	−3.20 (−22.94 to 41.12)	−8.77 (−36.12 to 12.25)	−49.39 (−60.41 to −25.46)
Diet high in sodium	8.93 (2.00 to 19.81)	−26.72 (−55.54 to −10.93)	0.98 (0.22 to 2.24)	−30.57 (−60.70 to 3.40)	11.19 (2.54 to 25.86)	−66.82 (−81.00 to −51.07)
Diet low in fiber	4.01 (−1.20 to 8.35)	−17.91 (−23.83 to −10.94)	0.43 (−0.13 to 0.91)	−29.03 (−39.30 to −13.66)	5.03 (−1.50 to 10.68)	−62.79 (−68.34 to −54.13)
Diet low in fruits	9.01 (−0.67 to 16.39)	−6.80 (−10.25 to −2.27)	0.97 (−0.07 to 1.82)	−17.90 (−28.77 to −0.63)	11.29 (−0.80 to 21.15)	−57.75 (−63.42 to −48.31)
Diet low in vegetables	1.44 (−0.16 to 2.99)	−12.35 (−27.08 to 0.82)	0.16 (−0.02 to 0.33)	−24.39 (−36.82 to −10.52)	1.82 (−0.19 to 3.81)	−60.01 (−66.55 to −52.45)
Secondhand smoke	4.66 (3.20 to 6.15)	−21.57 (−29.18 to −14.28)	0.51 (0.34 to 0.67)	−29.33 (−40.62 to −10.15)	5.84 (3.91 to 7.85)	−64.39 (−70.47 to −54.14)
Smoking	14.43 (12.36 to 16.45)	−24.05 (−33.60 to −6.70)	1.57 (1.28 to 1.90)	−31.23 (−44.19 to −4.46)	18.07 (14.72 to 21.86)	−65.67 (−72.32 to −51.79)
Environmental/ occupational risks	32.73 (25.80 to 39.46)	−24.89 (−31.47 to −17.71)	3.53 (2.64 to 4.59)	−30.29 (−43.65 to −5.99)	41.05 (30.76 to 53.24)	−65.95 (−72.61 to −53.59)
Ambient particulate matter pollution	14.20 (9.82 to 17.97)	44.32 (9.41 to 92.37)	1.53 (1.03 to 1.97)	34.74 (−1.61 to 87.79)	17.77 (11.98 to 22.81)	−34.50 (−52.60 to −8.18)
High temperature	1.13 (0.21 to 2.46)	79.32 (−116.49 to 446.78)	0.12 (0.02 to 0.27)	52.84 (−49.56 to 310.51)	1.43 (0.27 to 3.14)	−18.67 (−107.51 to 159.93)
Household air pollution from solid fuels	10.29 (5.50 to 17.36)	−59.68 (−75.02 to −40.14)	1.12 (0.58 to 1.96)	−62.11 (−77.49 to −40.99)	12.96 (6.67 to 22.68)	−81.68 (−89.17 to −71.32)
Lead exposure	6.18 (−0.81 to 13.75)	−14.54 (−19.14 to −7.03)	0.67 (−0.09 to 1.49)	−20.21 (−34.56 to 6.26)	7.76 (−1.03 to 17.25)	−61.32 (−68.44 to −48.24)
Low temperature	4.48 (3.76 to 5.27)	−27.51 (−32.60 to −22.58)	0.48 (0.39 to 0.58)	−34.82 (−46.98 to −13.73)	5.60 (4.62 to 6.77)	−67.19 (−73.42 to −56.35)
Metabolic risks	52.54 (38.93 to 63.50)	12.43 (5.88 to 20.57)	5.68 (4.15 to 7.12)	6.67 (−11.02 to 32.31)	65.78 (48.06 to 82.57)	−48.93 (−57.56 to −36.01)
High body mass index	4.92 (0.00 to 10.99)	233.52 (−671.23 to 1668.40)	0.53 (0.00 to 1.19)	199.02 (−624.52 to 1533.99)	6.14 (0.00 to 13.85)	53.22 (−346.64 to 686.75)
High systolic blood pressure	51.57 (37.95 to 62.61)	10.96 (4.62 to 18.43)	5.58 (4.05 to 7.06)	5.35 (−12.47 to 30.77)	64.58 (46.84 to 81.79)	−49.59 (−58.30 to −37.25)

Abbreviations: PAF, population attributable fraction; UI, uncertainty interval.

taxation, health education, cessation support, and prohibition of smoking in public places, and work environments including the hospitality industry represent evidence-based strategies that reduce smoking initiation and prevalence in populations.[38] Similarly, improvements in diagnostics, medications, and lifestyle interventions on weight, salt intake and diet, especially among people with a high risk of hypertension, are known to decrease the disease burden of high blood pressure.[39] In addition, the GBD 2021 estimates suggest that ambient and household air pollution have a comparable attribution to SAH burden with smoking which further highlights the importance of system-level disease prevention through policy changes rather than placing all burden on the individuals. Having said that, previous studies on the associations of air pollution and stroke risk have often clustered SAH with other stroke types and do not consider the potential confounding/mediating effects of other concurrent SAH risk factors.[37,40-44] Similar limitations occur in the evidence of many dietary factors,[45] including moderate to high consumption of alcohol.[31,32,37,46] Regarding high BMI, previous evidence suggests that after considering the indirect effects via smoking and hypertension, the independent role of BMI on SAH risk is negligible[47] but it may be associated with poor SAH outcomes.[48] As additional potential risk factors that were assessed for stroke in general but not for SAH in the GBD 2021 study, low physical activity[34,37,49-51] and adverse lipid profile[52,53] have also been associated with a higher risk of SAH whereas the independent effect of high blood glucose and diabetes on SAH risk is more controversial.[32,34,54,55]

Limitations

Even though the present study constitutes, to our knowledge, the most comprehensive analysis of the global, regional, and national burden estimates of SAH and their time trends, attributions to modifiable risk factors, and comparisons to other critical health outcomes, it also has limitations. First, due to the limited amount of SAH-specific data sources from various individual countries and population groups, many reported burden and risk factor estimates rely more on predictive covariates and assumptions of geographical similari-

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ties than actual high-quality observations. Given that the incidence and mortality estimates of SAH vary substantially both between[4-6] and within countries,[56-58] findings from population groups with limited or no actual data sources (eg, many individual countries) should be interpreted with caution and against other available evidence due to the increased risk of systematic selection, measurement, and detection biases. For example, of all 2910 SAH-specific data sources in the GBD 2021 study, only 22 originated from Sub-Saharan Africa including door-to-door prevalence surveys from Benin,[59] Ghana,[60] and Nigeria,[61] admission data from a rural Nigerian hospital,[62] and administrative cause-of-death registrations from Cape Verde, Ghana, South Africa, and Zimbabwe. Based on such scattered and sporadic data collections that invariably miss, eg, sudden-death SAHs without routinely conducted postmortem examinations, it seems probable that the GBD 2021 study underestimates the burden of SAH in many low-SDI regions from Sub-Saharan Africa. This lack of high-quality input data may also explain why female predisposition was not observed outside of high-SDI regions despite the consistent evidence from previous population-based studies.[5,32,63,64] Nevertheless, our findings about the exceptionally low burden of SAH in many low-SDI regions rather emphasize the importance of high-quality disease surveillance than support a favorable situation in these regions. Second, even though the GBD 2021 study uses numerous data sources across the world, the data from several relevant publications especially focusing on SAH risk factors have not been incorporated as part of its prediction models. In fact, all SAH-specific risk factor data sources of the GBD 2021 study focus on dietary risks or lead exposure, whereas the relative risk estimates of other exposures are based on the stroke literature in general. Therefore, the reliability of covariate-driven risk factor estimations of the GBD study could likely be improved by performing an updated systematic review gathering the most recent and relevant published risk factor data for SAH.[37] This would also enable the assessment of independent pathways and interactions of relevant SAH risk factors more comprehensively. Third, because the GBD 2021 study did not record the different etiologies of nontraumatic SAHs and most data sources were based on registration codes without external case validation, our findings should be applied cautiously to aneurysmal SAHs. Fourth, because the current GBD dataset did not include information about the regional and temporal changes in SAH diagnostics and treatment, future studies are still needed to determine the exact reasons for our epidemiological observations and establish pragmatic solutions for decreasing the global burden of SAH. For example, high-quality comparisons focusing on worldwide and temporal differences in prehospital, in-hospital, and posthospital care of SAH would be of great importance. Lastly, the current GBD data release included a limited number of data sources for the most recent years, particularly after the COVID-19 pandemic. Although no significant changes in the SAH burden were observed during the peak pandemic years of 2020 and 2021, future data releases may offer more comprehensive insights into the potential effects of COVID-19 and related shifts in health care systems on the global burden of SAH.

Conclusions

Despite decreasing age-standardized burden rates, SAH remains one of the most common cardiovascular and neurological causes of death and disability globally with constantly increasing absolute case numbers. Moreover, over 70% of the SAH-related burden appears to be attributed to modifiable risk factors, most importantly to high systolic blood pressure and smoking. Given the substantial and potentially preventable impact of SAH on global health, consideration of its distinct features from other stroke types in evidence-based public health planning, resource allocation, and prevention strategies is warranted. Besides efforts to decrease global hypertension and smoking rates, enhancing in-hospital patient care, the availability of diagnostic tools, neurosurgical tertiary care, and identification of UIAs among patients with a high SAH risk could serve as justified targets for future improvements, especially in low and middle SDI regions. At the same time, many countries, especially from Sub-Saharan Africa, do not have any SAH-specific data sources; this emphasizes the importance of international and interdisciplinary collaboration to produce more reliable burden estimates of SAH from these regions.

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